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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/641,742	DANISHEFSKY ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 56,58-62,65-67,69-76,78-81,84-86 and 88-98 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 56,58-62,65-67,69-76,78-81,84-86 and 88-98 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/18/00+7/1/09.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: IDS 9/18/03, 1/12/04, 1/31/05.

DETAILED ACTION

Acknowledgment is made of applicant's election of the species of Globo-H.

Claims 1-26, 33-38 40-55, 57, 63, 64, 68, 77, 82, 83 and 87 have been canceled. Claims 56, 58, 61, 62, 67, 69-74, 76, 78, 81, 86-88, 91-93, 95 and 97 have been amended. Claims 56, 58-62, 65-67, 69-76, 78-81, 84-86 and 88-98 are pending and under consideration. After review and reconsideration of the amended claims in light of the prior art, the species election requirement of the paper mailed May 18, 2005 is withdrawn.

Acknowledgement is made of applicant's claim to an earlier effective filing date via provisional application 60/150,088, filed August 20, 1999. After review of the '088 application it was concluded that it fails to provide support for the instant claims. The '088 application provide a written description of the synthesis of the fucosyl GM1 KLH conjugate (page 16) only. The provisional make no mention of a glycopeptide comprising a peptide backbone, or a glycopeptide which is multi-antigenic by virtue of being a cluster antigen or incorporation of distinct carbohydrate antigens into the same glycopeptide. Accordingly the instant claims are given priority only to the instant filing date of August 18, 2000.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 58 and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 58 and 78 recite "suitable" carrier protein or lipid, but fail to state the purpose by which to judge the suitability. Further suitability without further definition is a relative term because different practitioners can hold differing requirements for that which is "suitable".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56, 58-62, 65-67, 69-76, 78-81, 84-86 and 88-98 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claims 56, 76 have been amended to incorporate the limitation of "2 to 25" amino acid residues, wherein "two or more" of said amino acid is independently substituted. The originally filed specification fails to support this amendment. The specification as originally filed contemplates a linker which is a peptide fragment of 2 to 20 amino acids acyl residues (page 12, lines 14-15) which differs from the newly introduced limitation in that it requires acyl amino acids, and the upper limit is 20 amino acids, rather than 25. Further, the specification as originally filed contemplates a multi-antigenic glycopeptide made up of at least three glycoamino acids wherein one or more of said amino acids are substitutes with an allyl glycosidic moiety having the structure found on page 10. This differs from the newly introduced limitation which requires the substitution of "two or more amino acids" and does not include the limitation of at least one of said amino acids having the allyl glycosidic moiety set forth on page 10 of the specification and in claim 61, section a.

Claims 56, 58-62, 65, 67, 70-73, 76, 78-81, 84, 86, 89-92, 95, 97 and 98 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for multiantigenic glycopeptides comprising pyranose moieties, does not reasonably provide enablement for multi-antigenic glycopeptides comprising furanose moieties. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant claims are drawn in part to a carbohydrate determinate within which the values of "g" plus "i" is 1 or 2, the value of "d" plus "f" is one or two, and the value of "b" plus "c" is one or two. Claims 56 and 76 also state the bracketed structures can encompass furanose as well as pyranose moieties. In the event that "g" plus "i" is 1 or "d" plus "f" is one, or "b" plus "c" is one, the ring structures will be furanose moieties. The specification teaches that Globo-H, fucosyl GM1, KH-1, glycophorin, STN, LeY, N3, Tn, 2-6STn, (2,3)ST and TF are cancer carbohydrate antigens which are over-expressed at the surface of malignant cells in a variety of cancers (page 2, lines 4-8). All of the aforesaid cancer antigens are pyranose moieties. The specification does not teach cancer carbohydrate antigens which comprise furanose sugar moieties rather than the pyranose sugar moieties. While sugars lacking one carbon from those found in Globo-H, fucosyl GM1, KH-1, glycophorin, STN, LeY, N3, Tn, 2-6STn, (2,3)ST and TF are known in the art (for example, the abstract of Severin et al, Biokhimiya (Moscow), 1973, Vol. 38, pp. 583-588, the there are no cancer associated carbohydrates recognized in the art. The review article of Garg et al (Advances in Carbohydrate Chemistry and Biochemistry, 1994, Vol. 50, pp. 277-310) indicates in Table I, page 278, the amino acid-carbohydrate residue lineage found in mammals. It is noted that none of the carbohydrate residues would have a furanose

moiety. Further, the specification has failed to provide a synthetic methodology for a furanose polysaccharide derivative which would be required for reaction to the n-alkenyl group (section (a) of claim 61). It is concluded that one of skill in the art would be subject to undue experimentation is order to make a glycopeptide comprising the alkenyl glycoside structure and one of skill in the art would be subjected to undue experimentation without reasonable expectation of success in using said furanose polysaccharide without teachings of a type of cancer or pathological state which would be commensurate with the over-expression of a furanose polysaccharide on the cell surface.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 56, 58-61, 69, 76, 78-80, 88, 97 and 98 are rejected under 35 U.S.C. 102(a) as being anticipated by Danishefsky and Allen (Angew Chimie, March 3, 2000, Vol. 39, pp. 836-863, reference of the IDS filed July 1, 2002).

Claim 56 is drawn in part to a multi-antigenic glycopeptide, and wherein said multi-antigenic glycopeptide comprises 2 to 25 amino acid residues wherein two or more of said amino acids is independently substituted with a glycosidic moiety having carbohydrate determinants which are pyranose moieties. Claim 58 embodies the multi-antigenic glycopeptide of claim 56 wherein the glycopeptide is bound to a suitable carrier protein, peptide or lipid. Claim 59 embodies claim 58 wherein the carrier protein is BSA, poly-lysine of KLH. Claim 60 embodies claim 8, wherein the lipid is tripalmitoyl-S-glyceralcysteinylserine. Claim 61 embodies the multi-antigenic glycopeptide of claim 56 which is made by providing an alkenyl glycoside structure. However, it is noted that claim 61 is a product-by-process claim. The M.P.E.P. states

that product by process claims are not limited by the process steps, but by the characteristics of the product. Claim 69 embodies the glycopeptide of claim 56 wherein each occurrence of A is independently Globo-H, fucosyl GM1, KH-1, glycophorin, STN, LeY, N3, Tn, 2-6STn, (2,3)ST or TF. Claim 76 is drawn to a pharmaceutical composition comprising a multi-antigenic glycopeptide, and wherein said multi-antigenic glycopeptide comprises 2 to 25 amino acid residues wherein two or more of said amino acids is independently substituted with a glycosidic moiety having carbohydrate determinants which are pyranose moieties. Claim 78 embodies the pharmaceutical composition of claim 76 wherein the glycopeptide is bound to a suitable carrier protein or lipid. Claim 79 embodies claim 78 wherein the carrier protein is BSA or poly-lysine of KLH. Claim 80 embodies claim 78 wherein the lipid is tripalmitoyl-S-glyceralcysteinylserine. Claim 88 embodies the pharmaceutical composition of claim 76 wherein each occurrence of "A" is independently Globo-H, fucosyl GM1, KH-1, glycophorin, STN, LeY, N3, Tn, 2-6STn, (2,3)ST or TF. Claim 97 embodies the pharmaceutical composition of claim 76 wherein one or more or said imunological adjuvants is bacteria or liposomes. Claim 98 embodies claim 97 wherein the adjuvant is Salmonella minnesota, bacile Calmette-Guerin or QS-21.

Danishefsky and Allen disclose clustered glycopeptides, having a peptide backbone, wherein three amino acids are substituted with the glycosidic moieties of Tn, Tf, LeY (pages 855-859), and wherein the clustered glycopeptide is conjugated to a lipopeptide, KLH or BSA (page 856, first paragraph under "Discussion of Early Immunological Results"), thus fulfilling the specific embodiments of a . Danishefsky and Allen disclose the injection of the clustered immunoconjugate with an adjuvant such as tripalmitoyl-S-glyceralcysteinylserine and QS-21 ((page 856, first column, lines 1-3 and Table 3) fulfilling the specific embodiments of conjugated to a carrier and a composition comprising an immunological adjuvant. The clustered glycopeptides fulfill the specific embodiment of a multi-antigenic glycopeptide because each glycopeptide comprises three carbohydrate epitopes. The instant rejected claims do not specify that the multiple epitopes cannot be the same.

Claims 56, 58, 62, 69, 76, 78-81, 88-90 are rejected under 35 U.S.C. 102(a) as being anticipated by Danishefsky et al (WO 99/48515).

Claim 62 embodies the glycopeptide of claim 56 which is a construct have the structure of a glycopeptide attached to a linker which is attached to a crosslinker having an indicia of "q" wherein "q" can be 0 or 1, wherein said crosslinker is further attached to a carrier. Claim 89 embodies the pharmaceutical composition of claim 81 wherein the carrier is BSA, poly-lysine or KLH. Claim 90 embodies the pharmaceutical composition of claim 81 wherein the carrier is tripalmitoyl-S-glyceralcysteinylserine.

Danishefsky et al disclose the Tn trimer glycopeptide in Figure 20A, wherein said glycopeptide is conjugated to BSA, KLH or tripalmitoyl-S-glyceralcysteinylserine (compounds 3, 4 and 5 in Figure 20A). Danishefsy et al disclose the linker by which the attachment to the carrier is provided in Figure 20C which fulfills the specific embodiments of claim 62, wherein "q" is zero.

Claims 56, 61, 69, 76 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Toyokuni and Singha (Chemical Society Reviews, 1995, Vol. 24, pp. 231-242, reference of the IDS filed September 18, 2003).

Toyokuni and Singha disclose the Tn antigen cluster of Scheme 11, compound 19 (page 237) , which fulfill the requirement of a multi-antigenic glycopeptide because it contains three TN antigens attached to three amino acids. Toyokuni and Singha also fulfill the specific embodiments of claim 61 because the product would have the same structure as that made by the method of claim 61. Toyokuni and Singha disclose that a spacer was installed in order to preclude any interaction between the Tn antigens and the carrier molecule (page 235, second column, lines 3-5 under the heading "Linear Amplification"). Toyokuni and Singha disclose that compound 19 was linked to OSA (page 239, lines 1-3 under the heading of "Semi-Synthetic Tn Vaccines") thus fulfilling the specific embodiments of claims 76 and 78.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double-patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. In reBerg, 140 F.3d, 1428, 46 USPQ2d 1226 (Fed. Cir. 1998): In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993): In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Claims 56, 58-62, 65-67, 69-76, 78-81, 84-86 and 88-98 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 118-198 of copending Application No. 10/209,618 and claims 1-36 of copending Application No. 10/728,041. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the reference aplications anticipate the isntant claims..

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
10/3/2005

KAREN A. CANELLA PH.D
PRIMARY EXAMINER